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EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
03/02/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ip@akerman.com

Office Action Summary	Application No.	Applicant(s)	
	10/516,361	ISLAM ET AL.	
	Examiner	Art Unit	
	MARK STAPLES	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *159-181* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *159-181* is/are rejected.

7)☒ Claim(s) *171* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/04/2010 has been entered.

2. Applicant's cancellation of prior claims and submission of new claims in the paper filed on 02/04/2010 is acknowledged. Claims 1-158 are canceled.

Claims 159-181 consonant with species election of SEQ ID NOs: 19 and 25 (see Applicant Remarks filed 05/28/2009) are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections of Cancelled Claims Moot/ Withdrawn

3. The objections and rejections of canceled claims are moot and therefore are withdrawn.

New Rejections Necessitated by Amendment

New Claim Objection

4. Claim 171 is objected to because of the following informalities: for reciting the colloquial contraction "can't" when it appears that "cannot" is intended. Appropriate correction is required.

New Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 160 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 160 recites incompatible limitations on the length of the primers. Claim 160 recites that each of primer can be 40 nucleotides long (40 of 10-40) but the combined length of the two forward and reverse primers is 0 to 25 nucleotides long. How can a combined length of 80 be a length of 0 to 25? How can the combined length of the primers be 0?

7. Claims 163, 165, and 167 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 160 recites incompatible limitations on the length of the primers. The claims recite primers selected from previous claims but do not recite which of the primers of the previous claims are used.

Are all of the primers of the previous claims used or are some the primers used and is so which ones?

14. Claim 176 recites the term "including." This term has the same effect as using the phrase "such as." Regarding claim 8, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The scope of the claim is unclear, since it is not apparent if the scope is limited by what follows the term, or if the terms following the term "including" are actually a part of the claimed invention.

New Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 159-168, 171-176, and 178-180 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (United States Patent 5,866,336 issued 1999), Solinas et al. (Oct. 15, 2001) and Nazarenko et al. (2000, previously cited, hereinafter referred to as Nazarenko et al. (2000)),

Regarding claims 159, 162-165, 167, 171, 176, and 178, Nazarenko et al. teach methods of detection and quantification of a target nucleic acid sequence and/or a nucleic acid amplification reaction using a nucleic acid amplification (entire patent) comprising the step of:

having a Molecular Energy Transfer (MET)/Fluorescent Resonance Energy Transfer (FRET) between a donor MET/FRET moiety and an acceptor MET/FRET moiety separately on at least two separate oligonucleotides (see figures 7 and 8),

wherein the said moieties on two oligonucleotides are provided intnerllay in the oligonucleotides on a base at least 2 bases away from its 3' end for the acceptor (A) and the donor (D) is at least 1 base away from the 3' end (see Figures 7 and 8) is adapted to inhibit signal from primer dimer, and eliminate non-specific signal generation when the (MET/FRET moiety) labelled oligonucleotides are subjected to extension by a polymerase in a nucleic acid PCR amplification reaction with the target nucleic acid (see section *5.1.2* in column 23 and see section *5.4.1* in column 30), and

wherein a MET/FRET signal is generated from donor and acceptor on amplification of said target nucleic acid sequence when the MET/FRET moieties are

separated by 4-20 or 25 nucleotides in the amplification product by teaching that the donor and acceptor are separated by a range of about 3-20 nucleotides (see column 18 lines 43-59).

Regarding claim 159, Nazarenko et al. teach donor labels are internal in oligonucleotides and thus suggest but do not specifically teach the donor labels are internal by at least 2 bases from the 3' end of the oligonucleotide.

Regarding claim 161, Nazarenko et al. teach a third labeled oligonucleotide (see claim 20 and claim 3).

Regarding claim 168, Nazarenko et al. teach multiplex assays (see section *5.5* beginning in column 30).

Regarding claim 172, Nazarenko et al. teach FAM, rhodamine, and DABCYL (see claims 30 and 31 and see Table 1).

Regarding claim 179, Nazarenko et al. teach the sequence is from an infectious disease agent (see claim 10).

Regarding claim 180, Nazarenko et al. teach detection of mutated versus wild type heterozygous sequences (see claim 11).

Regarding claims 159, 162-165, 167, 171, 176, and 178, Solinas et al. teach methods of detection and/or quantification of a target nucleic acid sequence and/or a nucleic acid amplification reaction using a nucleic acid amplification (entire article) comprising the step of:

having a Molecular Energy Transfer (MET)/Fluorescent Resonance Energy Transfer (FRET) between a donor MET/FRET moiety and an acceptor MET/FRET moiety separately on at least two separate oligonucleotides (see Figure 5),

wherein the said moieties on two oligonucleotides are provided in the oligonucleotides on a base at least 2 bases away from its 3' end is adapted to inhibit signal from primer dimer, and eliminate non-specific signal generation when the (MET/FRET moiety) labelled oligonucleotides are subjected to extension by a polymerase in a nucleic acid PCR amplification reaction with the target nucleic acid (see Figure 5B where the internal donor FAM and an internal methyl red dA acceptor/quencher are each internal by at least 2 bases and see p. 7), and

wherein a MET/FRET signal is generated from donor and acceptor on amplification of said target nucleic acid sequence when the MET/FRET moieties are separated by 4-20 or 25 nucleotides in the PCR amplification product from PCR (see Figure 5 and see 2nd paragraph on p. 8).

Regarding claim 160 and 167, Solinas et al. teach primers which are 10-40 nucleotides in length (see Table 2).

Regarding claim 172, Solinas et al. teach FAM and ROX (see legend to Table 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the internally labeled oligonucleotides of Nazarenko et al. by placing the labels at least 2 bases away from the 3' ends as

suggested by Solinas et al. with a reasonable expectation of success. The motivation to do so is provided by Solinas et al. who teach that internal placement of donor and acceptor labels of primer dimer pairs is easily accomplished by labeling internal thymidines (see last sentence of the 1st paragraph on p. 7) and provides an intermolecular probe target interaction for fast and reliable detection of target nucleic acids (see last sentence of the 2nd paragraph on p. 1). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Regarding claim 159, Nazarenko et al. (2000) teach improved methods of detection and/or quantification of a nucleic acid target sequence by a nucleic acid amplification reaction (entire patent, specifically column 7 lines 14-21) with internal MET/FRET labels (see Figures 7 and 8) comprising:

(i) a first oligonucleotide sufficiently complementary to hybridize to a first nucleic acid strand of a target sequence and to act as a nucleic acid amplification primer, and a second oligonucleotide sufficiently complementary to hybridize to the complement of the said first nucleic acid strand and to act as a nucleic acid amplification primer in an appropriate reaction mixture by teaching:

> "The invention provides a method for detecting or measuring a product of a nucleic acid amplification reaction comprising: (a) contacting a sample comprising nucleic acids with at least two oligonucleotides, a first one of said oligonucleotides comprising a sequence complementary to a preselected target sequence that may be present in said sample, and said first one and a second of said oligonucleotides being a pair of primers adapted for use in said amplification reaction . . . " (see column 13 lines 27-34),

> "In another embodiment, the donor moiety is located on a first oligonucleotide and the acceptor is located on a second oligonucleotide" (see column 16 lines 23-26),
>
> and teach that the donor and acceptor can be MET moieties and FRET moieties which are a type of MET moieties and teach the MET/FRET distance is 10-100 Angstrom (see column 1 lines 14-16 lines 30-56) which is within the range of 10-80 Angstrom,
>
> and teach: "The target nucleic acid can be genomic or cDNA or mRNA or synthetic, human or animal, or of a microorganism . . (see column 20 lines 3-5);

the amplification reaction mixture containing the said sample and a polymerase, where the polymerase is a DNA polymerase (see claim 95) which can be Taq polymerase (see column 25 lines 12-16), wherein the said reaction mixture is subjected to an initial denaturation followed by repeated cycles of a combination of a denaturation step and at least a selective annealing step (taught throughout the patent, see for example column 56 lines 32-38 and see Figure 5 and its description at the bottom of column 8) ,

(ii) the said first and the second oligonucleotide primers do not form any combination in absence of an amplification reaction as they are hairpin primers , wherein the improvement comprises:

(ii) the presence of a target sequence in the sample being detected with improved sensitivity and specificity of the amplification product through the generation of a signal mainly on formation of a combination of the two primers and a combination of the two labels on the two separate primers on target amplification, and illuminating the PCR amplification reaction mixture in thin walled tubes with an UV transilluminator image analysis system (see Figure 23 and its description at column 11 lines 9-15).

Regarding claim 159, Nazarenko et al. (2000) teach donor labels are internal in oligonucleotides and thus suggest but do not specifically teach the donor labels are internal by at least 2 bases from the 3' end of the oligonucleotide.

Regarding claim 162 , 166, and 167, Nazarenko et al. (2000) teach providing a third oligonucleotide labeled with a third label moiety and teach first , second, and third oligonucleotide primers by teaching "a third nucleotide sequence of 6-30 nucleotides, wherein a nucleotide within said third nucleotide sequence is *labeled with a second moiety* [noting that this is the third label of the claims as Nazaneko et al. teach that their can be a second primer with different labels as given above and where label can internal on the oligonuceltoide, see claims 1-4 and Table 5] selected from the group consisting of said donor moiety and said acceptor moiety, and said second moiety is the member of said group not labeling said first nucleotide sequence, wherein said third nucleotide sequence is sufficiently *complementary* in reverse order to said *first nucleotide sequence* for a duplex to form between said first nucleotide sequence and said third nucleotide sequence such that said first moiety and second moiety are in sufficient proximity such that, when the donor moiety is excited and emits energy, the acceptor moiety absorbs energy emitted by the donor moiety; and (d) at the 3' end of said oligonucleotide, a fourth, single-stranded nucleotide sequence of 8-40 nucleotides that comprises at its 3' end a sequence sufficiently complementary to a preselected target sequence so as to be able to prime synthesis by a nucleic acid polymerase of a nucleotide sequence complementary to a nucleic acid strand comprising said target

sequence; wherein when said duplex is not formed, said first moiety and said second moiety are separated by a distance that prevents molecular energy transfer between said first and second moiety" (emphasis by Examiner, see column 20 lines 21-66, and see Figure 6 and see column 8 lines 60-65). Furthermore, Nazarenko et al. teach that multiple primers can be used in amplification and that each primer can be labeled with different fluorophores and/or different quenchers (see Table 1 for a list of FRET pairs and see column 17 lines 46-67). Furthermore, Nazarenko et al. teach that primers may be provided in semi-nested amplification which is a type of nested amplification (see column 4 lines 9-16). Even further, Becker et al. teach a third oligonucleotide can be used to nest between FRET primers (see Real-time PCR on p. 2563 and referencing Holland et al.).

Further regarding claims 162, Nazarenko et al Nazarenko et al. teach as noted above and teach amplification teach:

a primer labeled near the 3' end (see R of Fig. 7),

an unlabeled primer (see F of Fig. 7),

a third labeled oligonucleotide (see P of Fig. 7),

where the labeled primer is incorporated into the sequence (see Fig. 7) and where the labels are MET/FRET donor and acceptor and come within the MET distance on the target nucleic acid (as given above and see Fig. 7).

Regarding claim 168, Nazarenko et al. (2000) teach multiplexing of targets and labels (see column 36 lines 3-9).

Regarding claims 172-174, Nazarenko et al.(2000) teach donors and acceptors of fluorescein, DABCYL (see column 3 lines 3-17), and ethidium bromide (see column 10 line 30 and claim 37) which inherently is an intercalator and teach rhodamine (claim 23), carboxy fluorescein (calim 25), Malachite green (claim 40), and TEXAS RED® acceptor (claim 41).

Regarding claim 175, Nazarenko et al.(2000) teach biotin and avidin (see column 19 lines 50-57). Nazarenko et al. teach adding polymerase, reaction buffer, deoxy nucleoside triphosphates (dNTPs) in addition to the effective amounts of the amplification primers to the samples, cycling the sample between at least a denaturation temperature and an elongation temperature, exciting the reaction mixture with the donor exciting radiation or light, measuring the emission of the acceptor MET moiety (see column 35 lines 46 to column 36 line 61 and see column 38 lines 16-26).

Regarding claim 179, Nazarenko et al. where the target nucleic acid sequence is an amplficiation product of the infectious disease agent which is Chlamydia (see Table 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the MET/FRET methods of Nazarenko et al. and Solinas et al. with the intermediary acceptor of ROX, donor of FAM, and a general acceptor/quencher which specifically can be methyl red dA is by using ethidium bromide as an intermediary acceptor as suggested by Nazarenko et al. (2000) with a reasonable expectation of success. The motivation to do so is provided by Nazarenko

et al. (2000) who teach that ethidium bromide is a quencher and Solinas et al. who teach primer dimer pairs with an intermediary quencher prevents fluorescence cross talk and thus results in more specific detection of target nucleic acids (see last sentence on p. 7 continued to p. 8). Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to substitute ethidium bromide quencher as taught by Nazareko et al. (2000) for the quencher of Solinas et al. to arrive at the clamed invention. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

11. Claims 169, 170, and 177 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (1999), Solinas et al. (2001), and Nazarenko et al. (2000) as applied to claim 159 above, and further in view of Andersson et al. (2001, previously cited) and Chetverin et al. (1993, previously cited).

Nazarenko et al., Solinas et al. and Nazarenko et al. (2000) do not specifically teach a covalent linker to a solid support but teach the other limitations of claims 169 and 170 as found above and teach high throughput/multiplex methods.

Regarding claims 169, 170, and 177, Andersson et al. teaches attachment of probes/primers to solid supports (column 11 lines 55 and 56) which can be through a covalent linking moiety (column 11 line 15) and detection through FRET (see column 10 line 22) and where solid phase can be the translucent silica or glass polymers for amplification and detection of 5' end bound target nucleic acids as further taught by Chetverin et al. (see p. 8, 3rd paragraph and claims 36, 41, and 144).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Nazarenko et al., Solinas et al. and Nazarenko et al. (2000) by using linkers to solid supports as suggested by Andersson et al. and Chetverin et al. with a reasonable expectation of success. The motivation to do so is provided by Andersson et al. who teach that methods using the covalently bound probes of Chetverin et al. have enhanced sensitivity (column 11 lines 20 and 21). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

12. Claims 159-168, 171-176, and 178-180 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (United States Patent 5,866,336 issued 1999), Sato et al. (WO 1998/13524 published 2000) and Nazarenko et al. (2000, previously cited, hereinafter referred to as Nazarenko et al. (2000)).

Regarding claims 159, 162-165, 167, 171, 176, and 178, Nazarenko et al. teach methods of detection and quantification of a target nucleic acid sequence and/or a nucleic acid amplification reaction using a nucleic acid amplification (entire patent) comprising the step of:

having a Molecular Energy Transfer (MET)/Fluorescent Resonance Energy Transfer (FRET) between a donor MET/FRET moiety and an acceptor MET/FRET moiety separately on at least two separate oligonucleotides (see figures 7 and 8),

wherein the said moieties on two oligonucleotides are provided internally in the oligonucleotides on a base at least 2 bases away from its 3' end for the acceptor (A)

and the donor (D) is at least 1 base away from the 3' end (see Figures 7 and 8) is adapted to inhibit signal from primer dimer, and eliminate non-specific signal generation when the (MET/FRET moiety) labelled oligonucleotides are subjected to extension by a polymerase in a nucleic acid PCR amplification reaction with the target nucleic acid (see section *5.1.2* in column 23 and see section *5.4.1* in column 30), and

wherein a MET/FRET signal is generated from donor and acceptor on amplification of said target nucleic acid sequence when the MET/FRET moieties are separated by 4-20 or 25 nucleotides in the amplification product by teaching that the donor and acceptor are separated by a range of about 3-20 nucleotides (see column 18 lines 43-59).

Regarding claim 159, Nazarenko et al. teach donor labels are internal in oligonucleotides and thus suggest but do not specifically teach the donor labels are internal by at least 2 bases from the 3' end of the oligonucleotide.

Regarding claim 161, Nazarenko et al. teach a third labeled oligonucleotide (see claim 20 and claim 3).

Regarding claim 168, Nazarenko et al. teach multiplex assays (see section *5.5* beginning in column 30).

Regarding claim 172, Nazarenko et al. teach FAM, rhodamine, and DABCYL (see claims 30 and 31 and see Table 1).

Regarding claim 179, Nazarenko et al. teach the sequence is from an infectious disease agent (see claim 10).

Regarding claim 180, Nazarenko et al. teach detection of mutated versus wild type heterozygous sequences (see claim 11).

Regarding claims 159-165, 167, 171, 176, and 178, Sato et al. teach methods of detection and/or quantification of a target nucleic acid sequence and/or a nucleic acid amplification reaction using a nucleic acid amplification (entire publication) comprising the step of:

having a Molecular Energy Transfer (MET)/Fluorescent Resonance Energy Transfer (FRET) between a donor MET/FRET moiety and an acceptor MET/FRET moiety separately on at least two separate oligonucleotides (see Figure 5),

wherein the said moieties on two oligonucleotides are provided in the oligonucleotides on a base at least 2 bases away from its 3' end by teaching both donor and acceptor are from bases 4 to 20 in the hybrid (see paragraph 0034 and Figures 1B and 1D) and any 2' position of a ribose in the oligonucleotide may be labeled (see paragraph 0041 and Table 1 and see paragraphs 0096-0117 for examples of oligonucleotides labeled internally more 2 bases from the 3' end) is adapted to inhibit signal from primer dimer, and eliminate non-specific signal generation, and

wherein a MET/FRET signal is generated from donor and acceptor on amplification of said target nucleic acid sequence when the MET/FRET moieties are separated by 4 to 20 in the hybrid (see paragraph 0034 and Figures 1B and 1D).

Regarding claim 159, Sato et al. do not specifically teach extension.

Regarding claim 161, Sato et al. teach a third oligonucleotide (see paragraph 0038 description of Figure 1F).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the internally labeled oligonucleotides of Nazarenko et al. by placing the labels at least 2 bases away from the 3' ends as suggested by Sato et al. with a reasonable expectation of success. The motivation to do so is provided by Sato et al. who teach at length that the separation distance of the donor and quencher are important and the hybridized oligonucleotides can maintain this separation distance with internal labels of donor and quencher. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Regarding claim 159, Nazarenko et al. (2000) teach improved methods of detection and/or quantification of a nucleic acid target sequence by a nucleic acid amplification reaction (entire patent, specifically column 7 lines 14-21) with internal MET/FRET labels (see Figures 7 and 8) comprising:

(i) a first oligonucleotide sufficiently complementary to hybridize to a first nucleic acid strand of a target sequence and to act as a nucleic acid amplification primer, and a second oligonucleotide sufficiently complementary to hybridize to the complement of the said first nucleic acid strand and to act as a nucleic acid amplification primer in an appropriate reaction mixture by teaching:

> "The invention provides a method for detecting or measuring a product of a nucleic acid amplification reaction comprising: (a) contacting a sample comprising nucleic acids with at least two oligonucleotides, a first one of said oligonucleotides comprising a sequence complementary to a preselected target sequence that may be present in said sample, and said first one and a second of said oligonucleotides being a pair of primers adapted for use in said amplification reaction . . . " (see column 13 lines 27-34),
>
> "In another embodiment, the donor moiety is located on a first oligonucleotide and the acceptor is located on a second oligonucleotide" (see column 16 lines 23-26),
>
> and teach that the donor and acceptor can be MET moieties and FRET moieties which are a type of MET moieties and teach the MET/FRET distance is 10-100 Angstrom (see column 1 lines 14-16 lines 30-56) which is within the range of 10-80 Angstrom,
>
> and teach: "The target nucleic acid can be genomic or cDNA or mRNA or synthetic, human or animal, or of a microorganism . . (see column 20 lines 3-5);

the amplification reaction mixture containing the said sample and a polymerase, where the polymerase is a DNA polymerase (see claim 95) which can be Taq polymerase (see column 25 lines 12-16), wherein the said reaction mixture is subjected to an initial denaturation followed by repeated cycles of a combination of a denaturation step and at least a selective annealing step (taught throughout the patent, see for example column 56 lines 32-38 and see Figure 5 and its description at the bottom of column 8) ,

(ii) the said first and the second oligonucleotide primers do not form any combination in absence of an amplification reaction as they are hairpin primers , wherein the improvement comprises:

(ii) the presence of a target sequence in the sample being detected with improved sensitivity and specificity of the amplification product through the generation of a signal

mainly on formation of a combination of the two primers and a combination of the two labels on the two separate primers on target amplification, and illuminating the PCR amplification reaction mixture in thin walled tubes with an UV transilluminator image analysis system (see Figure 23 and its description at column 11 lines 9-15).

Regarding claim 159, Nazarenko et al. (2000) teach donor labels are internal in oligonucleotides and thus suggest but do not specifically teach the donor labels are internal by at least 2 bases from the 3' end of the oligonucleotide.

Regarding claim 162 , 166, and 167, Nazarenko et al. (2000) teach providing a third oligonucleotide labeled with a third label moiety and teach first , second, and third oligonucleotide primers by teaching "a third nucleotide sequence of 6-30 nucleotides, wherein a nucleotide within said third nucleotide sequence is *labeled with a second moiety* [noting that this is the third label of the claims as Nazaneko et al. teach that their can be a second primer with different labels as given above and where label can internal on the oligonuceltoide, see claims 1-4 and Table 5] selected from the group consisting of said donor moiety and said acceptor moiety, and said second moiety is the member of said group not labeling said first nucleotide sequence, wherein said third nucleotide sequence is sufficiently *complementary* in reverse order to said *first nucleotide sequence* for a duplex to form between said first nucleotide sequence and said third nucleotide sequence such that said first moiety and second moiety are in sufficient proximity such that, when the donor moiety is excited and emits energy, the acceptor moiety absorbs energy emitted by the donor moiety; and (d) at the 3' end of

said oligonucleotide, a fourth, single-stranded nucleotide sequence of 8-40 nucleotides that comprises at its 3' end a sequence sufficiently complementary to a preselected target sequence so as to be able to prime synthesis by a nucleic acid polymerase of a nucleotide sequence complementary to a nucleic acid strand comprising said target sequence; wherein when said duplex is not formed, said first moiety and said second moiety are separated by a distance that prevents molecular energy transfer between said first and second moiety" (emphasis by Examiner, see column 20 lines 21-66, and see Figure 6 and see column 8 lines 60-65). Furthermore, Nazarenko et al. teach that multiple primers can be used in amplification and that each primer can be labeled with different fluorophores and/or different quenchers (see Table 1 for a list of FRET pairs and see column 17 lines 46-67). Furthermore, Nazarenko et al. teach that primers may be provided in semi-nested amplification which is a type of nested amplification (see column 4 lines 9-16). Even further, Becker et al. teach a third oligonucleotide can be used to nest between FRET primers (see Real-time PCR on p. 2563 and referencing Holland et al.).

Further regarding claims 162, Nazarenko et al Nazarenko et al. teach as noted above and teach amplification teach:

a primer labeled near the 3' end (see R of Fig. 7),

an unlabeled primer (see F of Fig. 7),

a third labeled oligonucleotide (see P of Fig. 7),

where the labeled primer is incorporated into the sequence (see Fig. 7) and where the labels are MET/FRET donor and acceptor and come within the MET distance on the target nucleic acid (as given above and see Fig. 7).

Regarding claim 168, Nazarenko et al. (2000) teach multiplexing of targets and labels (see column 36 lines 3-9).

Regarding claims 172-174, Nazarenko et al.(2000) teach donors and acceptors of fluorescein, DABCYL (see column 3 lines 3-17), and ethidium bromide (see column 10 line 30 and claim 37) which inherently is an intercalator and teach rhodamine (claim 23), carboxy fluorescein (calim 25), Malachite green (claim 40), and TEXAS RED® acceptor (claim 41).

Regarding claim 175, Nazarenko et al.(2000) teach biotin and avidin (see column 19 lines 50-57). Nazarenko et al. teach adding polymerase, reaction buffer, deoxy nucleoside triphosphates (dNTPs) in addition to the effective amounts of the amplification primers to the samples, cycling the sample between at least a denaturation temperature and an elongation temperature, exciting the reaction mixture with the donor exciting radiation or light, measuring the emission of the acceptor MET moiety (see column 35 lines 46 to column 36 line 61 and see column 38 lines 16-26).

Regarding claim 179, Nazarenko et al. where the target nucleic acid sequence is an amplficiation product of the infectious disease agent which is Chlamydia (see Table 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the MET/FRET methods of Nazarenko et al. and Sato et al. with the acceptor of ROX, donor of FAM, and a general acceptor/quencher which is ethidium bromide as suggested by Nazarenko et al. (2000) with a reasonable expectation of success. The motivation to do so is provided by Nazarenko et al. (2000) who teach that ethidium bromide is a quencher and Sato et al. who teach primer dimer pairs with donor and quencher prevents fluorescence results in more specific detection of target nucleic acids. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to substitute ethidium bromide quencher as taught by Nazareko et al. (2000) for the quencher of Sato et al. or Nazarenko et al. to arrive at the clamed invention. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

13. Claims 169, 170, and 177 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (1999), Sato et al. (2000), and Nazarenko et al. (2000) as applied to claim 159 above, and further in view of Andersson et al. (2001, previously cited) and Chetverin et al. (1993, previously cited).

Nazarenko et al., Sato et al. and Nazarenko et al. (2000) do not specifically teach a covalent linker to a solid support but teach the other limitations of claims 169 and 170 as found above and teach high throughput/multiplex methods.

Regarding claims 169 and 170, Andersson et al. teaches attachment of probes/primers to solid supports (column 11 lines 55 and 56) which can be through a covalent linking moiety (column 11 line 15) and detection through FRET (see column 10 line 22) and where solid phase can be the translucent silica or glass polymers for amplification and detection of 5' end bound target nucleic acids as further taught by Chetverin et al. (see p. 8, 3rd paragraph and claims 36, 41, and 144).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of Nazarenko et al., Sato et al. and Nazarenko et al. (2000) by using linkers to solid supports as suggested by Andersson et al. and Chetverin et al. with a reasonable expectation of success. The motivation to do so is provided by Andersson et al. who teach that methods using the covalently bound probes of Chetverin et al. have enhanced sensitivity (column 11 lines 20 and 21). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Table 1 (re-provided)

100% Sequence Matches for SEQ ID Nos. 19 and 25

SEQ ID NO. 19

```
Application 10516361 and Search Result 20080724_093709_us-10-516-361b-19.rge.

Title:          US-10-516-361B-19
Perfect score:  20
Sequence:       1 ggggtactacagcgccctga 20

RESULT 5
LEIGPAA
LOCUS       LEIGPAA         3105 bp    DNA     linear   INV 26-APR-1993
DEFINITION  L.donovani.
```

```
ACCESSION   M60048
VERSION     M60048.1  GI:159334
KEYWORDS    glycoprotein 63.
SOURCE      Leishmania donovani
  ORGANISM  Leishmania donovani
            Eukaryota; Euglenozoa; Kinetoplastida; Trypanosomatidae;
            Leishmania.
REFERENCE   1  (bases 1 to 3105)
  AUTHORS   Webb,J.R., Button,L.L. and McMaster,W.R.
  TITLE     Heterogeneity of the genes encoding the major surface
glycoprotein
            of Leishmania donovani
  JOURNAL   Mol. Biochem. Parasitol. 48 (2), 173-184 (1991)
   PUBMED   1762629
COMMENT     Original source text: L.donovani DNA.
FEATURES             Location/Qualifiers
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                     /organism="Leishmania donovani"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:5661"
     gene            101. .1873
                     /gene="gp63"
     CDS             101. .1873
                     /gene="gp63"
                     /codon_start=1
                     /product="glycoprotein 63"
                     /protein_id="AAA29244.1"
                     /db_xref="GI:159335"

/translation="MSVDSSSTHRHRSVAARLVRLAAAGAAVIAAVGTAAAWAHAGAV

QHRCIHDAMQARVRQSVARHHTAPGAVSAVGLSYVTLGAAPTVVRAANWGALRIAVST

EDLTDSAYHCARVGQRISTRDGRFAICTAEDILTDEKRDILVKYLIPQALQLHTERLK

VRQVQDKWKVTGMGNEICGHFKVPPAHITDGLSNTDFVMYVASVPSEGDVLAWATTCQ

VFSDGHPAVGVINIPAANIASRYDQLVTRVVTHEMAHALGFSVVFFRDARILESISNV

RHKDFDVPVINSSTAVAKAREQYGCGTLEYLEMEDQGGAGSAGSHIKMRNAQDELMAP

ASDAGYYSALTMAIFQDLGFYQADFSKAEEMPWGRNAGCAFLSEKCMEDGITKWPAMF

CNENEVTMRCHTGRLSLGVCGLSSSDIPLPPYWQYFTDPLLAGISAFMDYCPVVVPFG

DGSCAQRASEAGAPFKGFNVFSDAARCIDGAFRPKTTETVTNSYAGLCANVRCDTATR

TYSVQVHGGSGYANCTPGLRVELSTVSSAFEEGGYITCPPYVEVCQGNVQAAKDGGNA
                     AAGRRGPRAAATALLVAALLAVAL"
ORIGIN

  Query Match             100.0%;  Score 20;  DB 12;  Length 3105;
  Best Local Similarity   100.0%;  Pred. No. 6.2;
```

```
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 GGGGTACTACAGCGCCCTGA 20
              ||||||||||||||||||||
Db       1114 GGGGTACTACAGCGCCCTGA 1133
```

SEQ ID NO. 25

From NCBI

```
LOCUS       LEIGPAA           3105 bp    DNA     linear   INV 26-APR-1993
DEFINITION  L.donovani.
ACCESSION   M60048
VERSION     M60048.1  GI:159334
KEYWORDS    glycoprotein 63.
SOURCE      Leishmania donovani
  ORGANISM  Leishmania donovani
            Eukaryota; Euglenozoa; Kinetoplastida; Trypanosomatidae;
            Leishmania.
REFERENCE   1  (bases 1 to 3105)
  AUTHORS   Webb,J.R., Button,L.L. and McMaster,W.R.
  TITLE     Heterogeneity of the genes encoding the major surface
glycoprotein
            of Leishmania donovani
  JOURNAL   Mol. Biochem. Parasitol. 48 (2), 173-184 (1991)
   PUBMED   1762629
COMMENT     Original source text: L.donovani DNA.
FEATURES             Location/Qualifiers
     source          1..3105
                     /organism="Leishmania donovani"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:5661"
     gene            101..1873
                     /gene="gp63"
     CDS             101..1873
                     /gene="gp63"
                     /codon_start=1
                     /product="glycoprotein 63"
                     /protein_id="AAA29244.1"
                     /db_xref="GI:159335"

/translation="MSVDSSSTHRHRSVAARLVRLAAAGAAVIAAVGTAAAWAHAGAV

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EDLTDSAYHCARVGQRISTRDGRFAICTAEDILTDEKRDILVKYLIPQALQLHTERLK

VRQVQDKWKVTGMGNEICGHFKVPPAHITDGLSNTDFVMYVASVPSEGDVLAWATTCQ
```

VFSDGHPAVGVINIPAANIASRYDQLVTRVVTHEMAHALGFSVVFFRDARILESISNV

RHKDFDVPVINSSTAVAKAREQYGCGTLEYLEMEDQGGAGSAGSHIKMRNAQDELMAP

ASDAGYYSALTMAIFQDLGFYQADFSKAEEMPWGRNAGCAFLSEKCMEDGITKWPAMF

CNENEVTMRCHTGRLSLGVCGLSSSDIPLPPYWQYFTDPLLAGISAFMDYCPVVVPFG

DGSCAQRASEAGAPFKGFNVFSDAARCIDGAFRPKTTETVTNSYAGLCANVRCDTATR

TYSVQVHGGSGYANCTPGLRVELSTVSSAFEEGGYITCPPYVEVCQGNVQAAKDGGNA
AAGRRGPRAAATALLVAALLAVAL"

ORIGIN

```
        1 cccacacgca cgcgcacacc gccgtgcaca agccctcgcc ctcgccctcg ccgtcgccac
       61 cacaccccac tgcccacagc gcccccgcgc ctgcagagcc atgtccgtcg acagcagcag
      121 cacgcaccgg caccgcagcg tcgccgcgcg cctggtgcgc ctcgcggctg ccggcgccgc
      181 agtcatcgct gctgtcggca ccgcggccgc gtgggcacac gccggtgcgg tgcagcaccg
      241 ctgcatccac gacgcgatgc aggcacgcgt gcggcagtcg gtggcgcgcc accacacggc
      301 ccccggcgcc gtgtccgcgg tgggcctgtc gtacgttact ctcggcgccg cgcccacagt
      361 cgtgcgcgcc gcgaactggg gcgcgctgcg catcgccgtc tccaccgagg acctcaccga
      421 ctccgcctac cactgcgctc gcgtcgggca gcgtattagc acgcgcgatg gccgcttcgc
      481 catctgcacc gccgaggaca tcctcaccga cgagaagcgc gacatcctgg tcaaatacct
      541 catcccgcag gcgctgcagc tgcacacgga gcggctgaag gtgcggcagg tgcaggacaa
      601 gtggaaggtg acgggcatgg gcaacgagat ctgtggccac ttcaaggtgc cgccggcgca
      661 catcaccgat ggcctgagca acaccgactt cgtgatgtac gtcgcctccg tgccgagcga
      721 gggggatgtg ctggcgtggg ccacgacctg ccaggtgttc tctgacggcc atccagccgt
      781 gggcgtcatc aacatccccg cggcgaacat tgcgtcgcgg tacgaccagc tggtgacgcg
      841 tgtcgtcacg cacgagatgg cgcacgcgct cggcttcagc gtcgtcttct tccgagacgc
      901 ccgcatcctg gagagcattt cgaacgttcg gcacaaggac ttcgatgttc ccgtgatcaa
      961 cagcagcacg gcggtggcga aggcgcgcga gcagtacggc tgcggcacct tggagtatct
     1021 ggagatggag gaccagggcg gtgcgggctc cgccgggtcg cacatcaaga tgcgcaacgc
     1081 gcaggacgag ctcatggcgc ctgcctcgga tgcggggtac tacagcgccc tgaccatggc
     1141 catcttccag gacctcggct tctaccaggc ggacttcagc aaggccgagg agatgccgtg
     1201 gggccggaac gccggctgcg ccttcctcag cgagaagtgc atggaggacg gcatcacgaa
     1261 gtggccggcg atgttctgca atgagaacga ggtgactatg cgctgccaca ccggtcgtct
     1321 cagccttggc gtgtgcggtt tatcctctag cgatattccc ttgccgccgt actggcagta
     1381 cttcacggac ccgctcctcg ccggcatctc cgccttcatg gactactgcc ctgtcgtggt
     1441 gcccttcggt gatggcagct gcgcgcagcg tgcgtctgaa gcgggcgcac cattcaaagg
     1501 cttcaacgtc ttctccgacg cggcgcgctg catcgatggc gccttcaggc cgaagacgac
     1561 cgaaaccgta acaaattcgt acgccggact gtgcgccaac gtgcggtgcg acacggccac
     1621 gcgcacgtac agcgtgcagg tgcacggcgg cagcggctac gccaactgca cgccgggcct
     1681 cagagttgag ctgagcaccg tgagcagcgc cttcgaggag ggcggctaca tcacgtgccc
     1741 gccgtacgtg gaggtgtgcc agggcaacgt gcaggctgcc aaggacggcg gcaacgccgc
     1801 ggctggtcgc cgtggtccgc gcgccgcggc gacggcgctg ctggtggccg cgctgctggc
     1861 cgtggcgctc tagacggtgg ataggacggg tggtgatggc gtgtcccctg ctccccccctc
     1921 cctccctccc tctcgttgtc tctcggaaga gctccacgct gtcctttcat ctcctcgcct
     1981 gttctacgct tgcttccgtg cgccgctgca ccgggccggt cctcgccgac cctcgcctgc
     2041 cctctccccc tcctctctcc cgccacccca ccccgcttcc cgctgcgcac ggtgcctgtg
     2101 cgcttggaga ggtgcagcag cgcgcgggag ctgagggagg gaggggggtgt cgtgcgcggg
     2161 tgcgcatgcc ttctttcact tccttatttg tcttctattt gttccctgcg acacccgcac
     2221 acccccaccc gctggcggcc atccgcggca tccgcgggtg cgtgcgcggt gtgtctgcct
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2401 tcccccattc gtgcgtgtct cttctcgctt tgtttttctg tttcctcttg tagcagggcg
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2521 gagtctcccg ccagcgcccg cgcagcgcag agccgtcgcc cacccaccgt ctcctcccac
2581 cttcgcatgc cgccgcacta ggtgcacgtc gtcggcacga ccaaccgagg tacctccccc
2641 cacccggcct ccggccccgc gcccctgcct ctgtgccgtg ccgtgccctg gactccctct
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2881 gcgctctccg ctctccctcc cccaccacct cccctcgcac cctcccttgc cctctccctg
2941 tcccctcccc ccccagatcc gccaacgcat ccgatcccgc tacaccctct cccccgccca
3001 cacgcacgcg cacaccgccg tgcacaagcc ctcgccctcg ccctcgccgt cgccaccaca
3061 ccccactgcc cacagcgccc ccgcgcctgc agagccatgt ccgtc
```

```
>gb|M60048.1|LEIGPAA  L.donovani
Length=3105
 Score = 40.1 bits (20),  Expect = 8e-06
 Identities = 20/20 (100%), Gaps = 0/20 (0%)
 Strand=Plus/Minus

Query  1     GTCCTGGAAGATGGCCATGG  20
             ||||||||||||||||||||
Sbjct  1153  GTCCTGGAAGATGGCCATGG  1134
```

14. Claim 181 is rejected under 35 U.S.C. 103(a) as being unpatentable over (1) Nazarenko et al., Solinas et al. and Nazarenko et al. (2000) as applied to claim 159 above, or (2) Nazarenko et al., Sato et al. and Nazarenko et al. (2000) as applied to claim 159 above; and further in view of Webb et al. (1993, previously cited) and Buck et al. (1998, previously cited).

Nazarenko et al., Solinas et al. and Nazarenko et al. (2000) teach as noted above.

Nazarenko et al., Sato et al. and Nazarenko et al. (2000) teach as noted above.

Regarding claim 181, Nazarenko et al. teach FAM and rhodamine (see claim 12) which can be used to label a primer.

With regard to claim 181, Nazarenko et al., Solinas et al., and Sato et al. and Nazarenko et al. (2000) disclose amplification of DNA with primers designed for amplification and detection as given above.

Nazarenko et al., Solinas et al., and Sato et al. and Nazarenko et al. (2000) teach primers and probes in general and teach various primer and probe sequences but do not specifically teach SEQ ID NOs: 19 or 25.

Webb et al. expressly disclose the identical nucleic acid sequences presented in SEQ ID NOs: 19 and 25 of the instant disclosure in Accession no. M60048 (see Table 1 above). It is noted that the instant primer sites of SEQ ID NOs: 19 and 25 are contained within the sequence disclosed by Webb et al.

The above described references of Nazarenko et al., Solinas et al., Sato et al., Nazarenko et al. (2000) and Webb et al. do not specifically disclose the identical primer sequences of SEQ ID NOs: 19 and 25 primers, respectively, used in the claimed invention.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers of the Accession no. M60048 and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck et al (1999) expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all

possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Conclusion

15. No claim is free of the prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Staples/
Primary Examiner, Art Unit 1637
February 24, 2010